



Universiteit
Leiden
The Netherlands

Organs-on-chip: towards therapies for cardiovascular disease using human stem cells

Helden, R.W.J. van

Citation

Helden, R. W. J. van. (2024, June 19). *Organs-on-chip: towards therapies for cardiovascular disease using human stem cells*. Retrieved from <https://hdl.handle.net/1887/3763914>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3763914>

Note: To cite this publication please use the final published version (if applicable).

ORGANS-ON-CHIP:
TOWARDS THERAPIES FOR CARDIOVASCULAR
DISEASE USING HUMAN STEM CELLS

Ruben W.J. van Helden

Colofon

Organs-on-chip: towards therapies for cardiovascular disease using human stem cells

This thesis was prepared at the Department of Anatomy & Embryology of the Leiden University medical Center, Leiden, The Netherlands. The work presented in this thesis was supported by the Netherlands Organ-on-Chip Initiative, an NWO Gravitation project (024.003.001) funded by the Ministry of Education, Culture, and Science of the government of The Netherlands and The Novo Nordisk Foundation Center for Stem Cell Medicine supported by Novo Nordisk Foundation grant (NNF21CC0073729).

Financial support from the Dutch Heart Foundation, the Willy van Heumenfonds, and Proefdier vrij for the publication of this thesis is gratefully acknowledged.

Additional financial support was also granted by nCardia Bv. and is greatly appreciated.

Cover design: Anna Sieben
Layout: Typesettr | www.typesettr.io
Printing: Ridderprint | www.ridderprint.nl
ISBN: 978-94-6506-110-8

Copyright © 2024 by Ruben W.J. van Helden, Vienna, Austria. All rights reserved. No part of this book may be reproduced, stored or transmitted in any form or by any means without prior permission of the author. The copyright of the publications remains with the publishers.

Organs-on-chip: towards therapies for cardiovascular disease using human stem cells

Proefschrift

ter verkrijging van

de graad van doctor aan de Universiteit Leiden,

op gezag van rector magnificus prof.dr.ir. H. Bijl,

volgens besluit van het college voor promoties

te verdedigen op donderdag 19 juni 2024

klokke 16:15 uur

door

Ruben Willem Joseph van Helden

geboren te 's-Gravenhage

in 1990

Promotor

Prof.dr. C.L. Mummery

Co-Promotor

Dr. M. Bellin

Dr. V.V. Orlova

Promotie commissie

Prof.dr. M.R.M. Jongbloed

Prof.dr. P. H.A. Quax

Prof.dr. P.C.J.J. Passier, TechMed Centre, Universiteit Twente

Prof.dr. J. van der Velden, Amsterdam UMC, Vrije Universiteit Amsterdam

TABLE OF CONTENTS

Chapter 1	General introduction – Towards therapies for mitochondrial cardiomyopathies using advanced human stem cell models	7
Chapter 2	Generation of three human induced pluripotent stem cell lines, LUMCi024-A, LUMCi025-A, and LUMCi026-A, from two patients with Combined Oxidative Phosphorylation Deficiency 8 and a related control	25
Chapter 3	Disrupted energetics and contraction in cardiomyocytes with infantile mitochondrial cardiomyopathy	39
Chapter 4	Generation, functional analysis and applications of isogenic three-dimensional self-aggregating cardiac microtissues from human pluripotent stem cells	83
Chapter 5	On-chip analysis of glycolysis and mitochondrial respiration in human induced pluripotent stem cells	171
Chapter 6	General discussion	197
Appendices	Nederlandse samenvatting	210
	Curriculum vitae	213
	List of publications	214
	Dankwoord	215